UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/935,966	08/23/2001	James J. Rahal	13099	1546

7590 06/01/2004

William D. Schmidt
Kalow & Springut LLP
19 th Floor
488 Madison Avenue
New York, NY 10022

EXAMINER	
WINKLER, ULRIKE	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 06/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/935,966	RAHAL, JAMES J.	
	Examiner	Art Unit	
	Ulrike Winkler	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *1-4 and 10-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-9 and 17-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed March 18, 2004 in response to the Office Action of October 21, 2003 is acknowledged and has been entered. Claims 5-9 and newly added claims 17-24 are pending and are currently being examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 103

The rejection of claims 7-9 under 35 U.S.C. 103(a) as being unpatentable over Crance et al. (Travaux, 1999, see applicants IDS) in view of Albrecht et al. (U.S. Pat. No. 6,387,365) **is withdrawn** in view of Applicants amendments and arguments.

New rejection in view of applicant's amendment to the claims:

Claims 5-9 and newly added claim 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crance et al. (Travaux, 1999, see applicants IDS) in view of Albrecht et al. (U.S. Pat. No. 6,387,365), Takahashi et al. (Antiviral Research, 1998) and Gkecil et al. (Journal of Neurological Science, 1999).

Applicants arguments to the prior rejection citing only Crance et al. and Albrecht et al. have been fully considered but fail to fully persuade the Office. Applicants arguments are that the claims are clearly drawn to effects of West Nile virus on the central nervous system and that the prior art (citing Smith et al.) indicated that administration of interferon alpha-2b to an animal would not result in a sufficient concentration of interferon alpha-2b in the central nervous system

to be effective. The cited Smith et al. indicates that interferon alpha-2b will not result in measurable concentration of interferon alpha-2b in the cerebrospinal fluid.

The amended claims are drawn to a method of treating or preventing meningitis, encephalitis or meningo-encephalitis caused by West Nile virus infection in an animal using an effective amount of interferon alpha-2b. The claims are drawn to administration of the interferon to an animal, the claims do not make a limitation regarding the route of administration.

Crance et al. disclose the effect of known antiviral agents on a select group of flaviviruses including West Nile virus. The composition tested in the reference is interferon alpha-2b here the antiviral agent is added to the cell line at the same time the virus is added. Table 1 indicates that treatment at a dose of 10 IU /ml is sufficient to inhibit West Nile cyotpathogenic effect. The reference does not administer the antiviral compound to a patient, however, the reference indicates that this is the goal of the study.

Albrecht et al. teaches the use interferon alpha-2b for the treatment of chronic hepatitis C a flavivirus. In prior treatment of chronic hepatitis C infection with .alpha.-IFN monotherapy, .alpha.-IFN has been administered in dosages of about 3 to 10 million International units (IU) thrice weekly. Alternatively 3 to 10 million IU of .alpha.-IFN has been administered QOD (every other day) or daily. The duration of the prior dosages has been from 12 to 24 months. This amount and duration of .alpha.-IFN monotherapy alleviates symptoms of hepatitis C in some of the patients, but it causes undesirable side effects, e.g. flu-like symptoms, in some (see column 2 lines 23-31). The preferred method of administering the .alpha.-IFN is parenterally, preferably by subcutaneous, IV, or IM, injection (see column 2, lines 55-56). The reference does not teach treating West Nile virus infection with interferon alpha-2b.

Takahashi et al. teach the administration of interferon alpha via intracranial route to hamsters suffering from subacute sclerosing panencephalitis.

Gokcil et al. disclose the administration of interferon alpha to human patients via the Ommaya reservoir, a device that allows for the administration of drugs directly into the central nervous system, for the treatment of subacute sclerosing panencephalitis.

It would have been obvious to one of ordinary skill in the art to apply the interferon alpha-2b monotherapy treatment as taught by Albrecht et al. for the treatment of West Nile virus infection as taught by Crance et al. One having ordinary skill in the art would have a high expectation of success in administering interferon alpha-2b to a patient with West Nile virus in view of the teaching of Crance et al. which indicates that interferon alpha-2b is highly effective at preventing viral replication in the cell culture as established by the reduction of the cytopathic effect. Since the interferon alph-2b treatment can be administered at sufficient doses to achieve an effective treatment *in vivo* in a human patient with hepatitis C infection, another flavivirus infection, the ordinary artisan would have a high expectation of success in applying the same antiviral agent to a West Nile virus infection *in vivo*. Both Takahashi et al. and Gokcil et al. teach the use of interferon alpha for the treatment of a viral infection affecting the brain. Based on what is known in the prior art regarding West Nile virus it would have been *prima facie* obvious to administer interferon-alpha 2b directly to the central nervous system in order to exert the effect of the drug. Therefore, the instant invention is obvious over Crance et al. in view of Albrecht et al. and further in view of Takahashi et al. (Antiviral Research, 1998) and Gkecil et al. (Journal of Neurological Science, 1999).

Claim Rejections - 35 USC § 112

Claims 5, 7-9, 17-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The amended claims are drawn to a method of treating or preventing meningitis, encephalitis or meningo-encephalitis caused by West Nile virus infection in an animal using an effective amount of interferon alpha-2b. The route of administration is parenterally, ie. intravenous, subcutaneous, intramuscularly or mucosal.

The composition interferon alpha 2b may not reach the target because of its inability to penetrate tissues or cells where its activity is to be exerted (brain), may be absorbed by fluids, cells and tissues where the composition has no effect, circulation into the target area may be insufficient to carry the composition and a large enough local concentration may not be established. Applicants pointed out in the response to the prior 35 U.S.C. 103(a) (above) that according to the Smith et al. (Clinical Pharmacological Therapy, 1985) there is no indication of achieving a concentration of interferon alpha-2b in the cerebrospinal fluid to be in an amount effective for the treatment of a West Nile virus infection. A review of the specification indicates that the only real examples provided (Table 1, page 11) is the suppression of WNV in cell cultures. The *in vivo* studies are merely contemplated in examples 2 and 3. Therefore, applicants disclosure does not overcome the problem cited in the prior art of administration of interferon alpha 2b in such a way that will result in a high enough concentration of the interferon alpha 2b unless it is administered directly to the brain [see Takahashi et al., Antiviral Research,

1998 and Gkecil et al., Journal of Neurological Science, 1999]. Furthermore, there is a question of neurotoxicity when administering interferon alpha [see Merimsky et al., Anticancer Drugs 1992] these effects include confusion, fatigue, lethargy, cortical blindness or coma, when administered either intramuscularly or intravenously. These symptoms seem to be more common in the elderly, the same patient population that is most effected by WNV infection.

There is lack of enablement for the the administration of interferon alpha-2b via the parenteral route to result in the (1) treatment of meningitis, encephalitis or meningo-encephalitis caused by West Nile virus infection or (2) prevention of meningitis, encephalitis or meningo-encephalitis caused by West Nile virus infection. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure how to administer interferon alpha 2b in an effective amount to a patient so that the drug reaches the affected part (brain). Therefore, in view of the speculative nature of the invention, the lack of predictability of the prior art, the breadth of the claims and the absence of working examples, it would require undue experimentation for one skilled in the art to practice the invention as claimed.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989). The Group 1600 Official Fax number is: (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center representative whose telephone number is (571)-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 571-272-0912. The examiner can normally be reached M-F, 8:30 am - 5 pm. The examiner can also be reached via email [ulrike.winkler@uspto.gov].

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 571-272-0902.

ULRIKE WINKLER, PHD.
PATENT EXAMINER 5/28/04